

Claims

1. An agent for improving the blood stability of a mammalian endogenous ligand, which comprises an antibody that has an
5 affinity to the endogenous ligand but does not neutralize the same substantially.
2. The agent of claim 1, wherein the improved blood stability of the endogenous ligand results in the enhancement of receptor
10 activity-regulatory action thereof.
3. The agent of claim 1, wherein the neutralizing activity of the antibody is about 80% or less.
- 15 4. The agent of claim 1, wherein the blood concentration of the endogenous ligand becomes about twice or more compared to the case where the antibody is not administered.
5. The agent of claim 1, wherein the blood half-life of the
20 complex of the endogenous ligand and the antibody is about twice or more as that of the endogenous ligand alone.
6. The agent of claim 1, wherein the blood half-life of the free endogenous ligand is about one week or less.
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7. The agent of claim 1, wherein the endogenous ligand is a peptidic compound.
8. The agent of claim 7, wherein the endogenous ligand is one
30 against a G protein-coupled receptor.
9. The agent of claim 8, wherein the endogenous ligand is one belonging to secretin/glucagon super family.
- 35 10. The agent of claim 9, wherein the endogenous ligand is

selected from the group consisting of GLP-1, calcitonin, PACAP, VIP and analogs thereof.

11. The agent of claim 8, wherein the endogenous ligand is
5 selected from the group consisting of LHRH, metastin, GPR7/GPR8 ligand, MSH, ghrelin, apelin and analogs thereof.

12. The agent of claim 7, wherein the endogenous ligand is
selected from the group consisting of EPO, TPO, insulin,
10 interferon, growth hormone, GM-CSF, leptin, adiponectin and analogs thereof.

13. The agent of claim 7, wherein the endogenous ligand is
selected from the group consisting of ANP, BNP, CNP,
15 betacellulin, betacellulin- δ 4, adrenomedullin and analogs thereof.

14. The agent of claim 1, which is for the prophylaxis and/or
treatment of a disease in which an increased blood
20 concentration and/or a prolonged blood half-life of the
endogenous ligand are/is effective for the prophylaxis and/or
treatment thereof.

15. The agent of claim 14, wherein the disease is selected from
25 the group consisting of metabolic disease, bone and joint
disease, cardiovascular disease, cranial nerve disease,
infectious disease, cancer, blood disorder, urologic disease,
infertility/erectile dysfunction, deficient growth and
immunodeficiency.

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16. A method for the prophylaxis and/or treatment of a disease
in a mammal, wherein an increased blood concentration and/or a
prolonged blood half-life of an endogenous ligand are/is
effective for the prophylaxis and/or treatment of the disease,
35 which method comprises administering to the mammal an effective

amount of an antibody that has an affinity to the endogenous ligand but does not neutralize the same substantially, without administering a compound the same as or substantially the same as the endogenous ligand, so as to increase the blood stability⁵ of the endogenous ligand, thereby enhancing a receptor activity-regulatory action of the ligand.

17. A use of an antibody that has an affinity for an endogenous ligand but does not neutralize the same substantially for the¹⁰ manufacture of an agent for the prophylaxis and/or treatment of a disease in which an increased blood concentration and/or a prolonged blood half-life of the endogenous ligand are/is effective for the prophylaxis and/or treatment thereof.